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# Long-Term Exposure to Particulate Matter and Self-Reported Hypertension: A Prospective Analysis in the Nurses' Health Study

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**Short title:** Long-term particulate matter and hypertension

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## ABSTRACT

**Background:** Studies have suggested associations of elevated blood pressure with short-term air pollution exposures, but the evidence is mixed regarding long-term exposures on incidence of hypertension.

**Objectives:** We examined the association of hypertension incidence with long-term residential exposures to ambient particulate matter and residential distance to roadway.

**Methods:** We estimated 24-month and cumulative average exposures to PM<sub>10</sub>, PM<sub>2.5</sub>, and PM<sub>2.5-10</sub> and residential distance to road for women in the prospective nationwide Nurses' Health Study. Hazard ratios and 95% confidence intervals were calculated for incident hypertension 1988-2008 in Cox proportional hazards models, adjusted for potential confounders. We considered effect modification by age, diet, diabetes, obesity, region, and latitude.

**Results:** Among 74,880 participants, 36,812 incident cases of hypertension were observed during 960,041 person-years. In multivariable models, 10  $\mu\text{g}/\text{m}^3$  increases in 24-month average PM<sub>10</sub>, PM<sub>2.5</sub>, and PM<sub>2.5-10</sub> were associated with small increases in the incidence of hypertension (HR: 1.02, 95%CI: 1.00, 1.04; HR: 1.04 95%CI: 1.00, 1.07; and HR: 1.03, 95%CI: 1.00, 1.07, respectively). Associations were stronger among women under 65 years of age (HR: 1.04, 95%CI: 1.01, 1.06; HR: 1.07 95%CI: 1.02, 1.12; and HR: 1.05, 95%CI: 1.01, 1.09, respectively) and the obese (HR: 1.07, 95%CI: 1.04, 1.12; HR: 1.15 95%CI: 1.07, 1.23; and HR: 1.13, 95%CI: 1.07, 1.19, respectively), with p-values for interaction <0.05 for all models except age and PM<sub>2.5-10</sub>. There was no association with roadway proximity.

**Conclusions:** Long-term exposure to particulate matter was associated with small increases in risk of incident hypertension, especially among younger women and the obese.

## INTRODUCTION

Both short-term and long-term exposures to particulate matter (PM) have been shown to be associated with cardiovascular morbidity and mortality in epidemiological studies (Dockery et al. 1993; Hart et al. 2015; Hoek et al. 2013; Laden et al. 2006; Pope et al. 2002; Puett et al. 2008). The mechanisms underlying these associations have been hypothesized to include combinations of autonomic nervous system alterations, systemic inflammation, vascular reactivity, and endothelial dysfunction (Brook et al. 2004; Brook et al. 2010). These mechanisms may also be related to changes in blood pressure and subsequent risk of hypertension. A growing number of studies have observed that short-term exposures to PM are associated with elevations in systolic and/or diastolic blood pressure, and emergency department visits for hypertension within several hours to days after air pollution exposure (Arbex et al. 2010; Auchincloss et al. 2008; Chen et al. 2012; Chuang et al. 2010; Dai et al. 2016; Dvonch et al. 2009; Giorgini et al. 2015; Guo et al. 2010; Ibaldo-Mulli et al. 2001; Mar et al. 2005; Szyszkowicz et al. 2012; Wu et al. 2013). A number of studies have also shown associations between long-term exposures to air pollution and blood pressure (Chan et al. 2015; Chuang et al. 2011; Foraster et al. 2014b; Liu et al. 2016; Schwartz et al. 2012).

The evidence for air pollution impacts on hypertension is more inconsistent. Most, but not all, studies from China, Taiwan, and Europe have reported increasing prevalence of hypertension with exposures to particulate matter (PM) and nitrogen oxides (Babisch et al. 2014; Chen et al. 2015; Dong et al. 2013; Foraster et al. 2014a; Foraster et al. 2014b; Fuks et al. 2011; Fuks et al. 2014; Hoek et al. 2013; Sorensen et al. 2012; Zhao et al. 2013). To date, only two studies have examined the association between exposures to air pollution and incident hypertension. Two

analyses have been conducted in the Black Women's Health Study, with positive associations observed for PM exposures among participants living in Los Angeles, but no associations observed in the full cohort (Coogan et al. 2012; Coogan et al. 2015). Positive associations were also observed using information from population-based health surveys in Ontario, Canada (Chen et al. 2014).

In this study, we sought to examine the role of chronic exposures to PM 2.5  $\mu\text{m}$  or less in aerodynamic diameter (PM<sub>2.5</sub>), PM between 2.5 and 10  $\mu\text{m}$  (PM<sub>2.5-10</sub>), PM less than 10  $\mu\text{m}$  (PM<sub>10</sub>), and proximity to major roadways (a proxy for traffic exposure) as risk factors for incident hypertension in the Nurses' Health Study (NHS), after controlling for a number of time-varying hypertension risk factors. We also explored if the associations were modified by a number of lifestyle and exposure related factors to determine if differences in the proportions of susceptible subpopulations may explain the heterogeneity of findings in the literature.

## **METHODS**

### **Study population and outcome assessment**

The Nurses' Health Study (NHS) is an ongoing prospective cohort of 121,700 female registered nurses who were between 30-50 years of age at the beginning of the study in 1976. The participants originally lived in 11 states (New York, California, Florida, Massachusetts, Pennsylvania, Texas, Ohio, New Jersey, Michigan, Connecticut, and Maryland) but as of the 1990s at least 10 nurses resided in each state in the contiguous US. Since the study's inception, each participant completes a questionnaire every two years, providing information on risk factors, health outcomes, and residential address. From 1976 until the present, only 6% of nurses

available for follow-up no longer respond to questionnaires. All nurses alive, still responding to questionnaires, and free of hypertension in 1988 (the first year pollution measures were available) were eligible for the current analysis if they had an address in the continental US where exposure could be assessed. This study was approved by the institutional review board of the Brigham and Women's Hospital and informed consent was implied by return of the questionnaires.

On each questionnaire, women are asked to report any diagnoses they have received since the last questionnaire. Participants were considered to have hypertension if they reported hypertension on the questionnaire ("physician diagnosis of high blood pressure"). In a validation study (n=100) using medical records to confirm systolic or diastolic BP>140 or >90 mmHg, agreement between the medical record and self-report was almost 100% (Colditz et al. 1986).

### **Exposure assessment**

Geographic information system (GIS)-based spatio-temporal models were used to predict monthly exposures to PM<sub>10</sub> and PM<sub>2.5</sub> for each participant residing in the contiguous US between January 1988 and December 2007. The methods for estimating these exposures have been previously validated and discussed in detail elsewhere (Yanosky et al. 2014). In brief, we used data from the US Environmental Protection Agency's (USEPA) Air Quality System (AQS), the Interagency Monitoring of Protected Visual Environments (IMPROVE) networks and several Harvard-based research studies, as well as data from various other sources to create separate PM prediction surfaces for each PM size fraction for each month. A geographic information system (GIS) was used to generate a number of geospatial predictors including: roadway proximity,

percent urban land use within 1 km, smoothed county population density, tract population density, elevation, point sources of PM, and a number of meteorological predictors (Yanosky et al. 2014). As EPA AQS monitoring data for PM<sub>2.5</sub> was not available prior to 1999, separate PM<sub>2.5</sub> models were developed for pre-1999 and post-1999 periods (Yanosky et al. 2014). PM<sub>2.5</sub> in the period before 1999 was modeled using data on PM<sub>10</sub>. We also obtained data on PM<sub>2.5-10</sub> by subtraction of the monthly PM<sub>10</sub> and PM<sub>2.5</sub>. Cross-validation results demonstrated that there was little bias and a high degree of precision, when comparing the predicted and observed values (Yanosky et al. 2014). We averaged the monthly-specific exposures to PM<sub>10</sub>, PM<sub>2.5</sub> and PM<sub>2.5-10</sub> to create two time-varying exposure metrics; a 24-month moving average and a cumulative average including all predictions from 1988 through the current time period. The 24-month average was chosen to match the reporting periods for hypertension, and was calculated using the same 24-months for all nurses in each biennial cycle.

Roadway proximity was used as a proxy for traffic-related air pollution exposures. We calculated distance (in meters) for each residential address using GIS (ArcGIS, version 9.2; ESRI). ESRI StreetMap Pro 2007 road segments were selected to include the three largest US Census Feature Class Codes: A1 (primary roads, typically interstate highways, with limited access, division between the opposing directions of traffic, and defined exits), A2 (primary major, non-interstate highways and major roads without access restrictions), or A3 (smaller, secondary roads, usually with more than two lanes). According to the distribution of roadway proximity in this cohort and previous studies showing exponential decay in exposures with increasing distance, we created the following categories for all roads segments combined (A1-A3): 0-99 m, 100-199 m, over 200 m (Adar and Kaufman 2007; Hart et al. 2009; Karner et al. 2010; Lipfert and Wyzga

2008; Puett et al. 2009). We also examined these distance categories for each type of road segment separately, for the two largest road types (A1-A2), and considered continuous measures of exposure. To determine the robustness of our findings to cut point selection, we examined additional categorizations (e.g. 0-49 m, 50-99 m, 100-199 m, 200-499 m, 500+m; 0-49 m, 50-99 m, 100-199 m, 200-499 m, 500-999 m, 1000+ m).

### **Potential confounders and effect modifiers**

Information on potential confounders and effect modifiers were available from each biennial questionnaire (every other questionnaire for dietary information and physical activity) and were modeled as time-varying (with the exception of race). We selected *a priori* variables that have previously been associated with hypertension or exposure to PM in this cohort as potential confounders: race, physical activity in metabolic equivalent hours per week (MET hr/week), alcohol consumption (g/day), smoking status (current, former, never) and pack-years, body mass index (BMI; kilograms per meter squared), family history of hypertension, physician diagnosed diabetes, hypercholesterolemia, menopausal status, non-narcotic analgesic intake (NSAIDs, acetaminophen, aspirin), and current use of statins. The Dietary Approaches to Stop Hypertension (DASH) score (Bhupathiraju and Tucker 2011) was calculated from each of the semi-quantitative food frequency questionnaires. Census-tract median household value and median family income were considered as measures of area level socioeconomic status (SES). Individual-level SES measures included educational attainment, marital status and partner's educational attainment, and occupation of the nurses' mother and father. There is some epidemiologic evidence of increasing blood pressure with increasing latitude, which is hypothesized to be due to reduced UV exposures, colder weather, or differences in flora and

fauna (He et al. 1995; Rostand 1997). Therefore, in addition to region of residence (Northeast, South, Midwest, and West) to adjust for potential regional differences in pollution sources and diagnostic patterns, we also controlled for latitude ( $0^{\circ}$ - $20^{\circ}$ ,  $20^{\circ}$ - $40^{\circ}$ ,  $40^{\circ}$ - $60^{\circ}$ ). To assess the impact of each potential confounder, we added each variable or set of variables to the basic model including age, race, calendar year, and region of residence. Variables that are known risk factors for hypertension and those that led to at least a 10% change in the main effect estimate were included in the final multivariable models. Effect modification by age, diabetes, obesity ( $\text{BMI} \geq 30 \text{ kg/m}^2$ ), DASH score, region, latitude, time period (dichotomized at 2000), and if the participant moved in the last questionnaire cycle were evaluated through stratification and statistical significance was assessed using multiplicative interaction terms.

### **Statistical analysis**

Time varying Cox proportional hazards models on a biennial time scale, stratified by age in months and two-year calendar period (to tightly adjust for trends over time), were used to model the relationship of incidence of hypertension with the predicted  $\text{PM}_{2.5}$ ,  $\text{PM}_{10}$ ,  $\text{PM}_{2.5-10}$  exposure measures. We calculated hazard ratios (HRs) and 95% confidence intervals (95% CIs) for a  $10\text{-}\mu\text{g/m}^3$  increase in each size fraction separately, and, after examining the correlations between size fractions, in models including both  $\text{PM}_{2.5-10}$  and  $\text{PM}_{2.5}$ . We also assessed associations of hypertension with roadway proximity using continuous and categorical variables. The linearity of all continuous exposure-response functions was assessed using cubic regression splines. Person-months of follow-up time were calculated from baseline (30 Jun 1988) until self-reported hypertension, censoring (loss of follow-up, moving outside the contiguous US), death, or end of follow-up (30 Jun 2008), whichever came first.

## RESULTS

During the full period of follow-up, the mean age was approximately 61 years, most of the participants were never (44%) or former smokers (41%) and 56% had a BMI under 25 (Table 1). Mean ( $\pm$ SD) levels of PM<sub>10</sub>, PM<sub>2.5</sub> and PM<sub>2.5-10</sub> exposures in the previous 24 months were 22.24 $\pm$ 6.64, 15.61 $\pm$ 4.24, and 10.56 $\pm$ 4.80  $\mu$ g/m<sup>3</sup>, respectively. The correlations between exposures are shown in Table 2. Overall, the two exposure averaging periods were highly correlated for each of the size fractions of PM. The correlations between exposures varied – PM<sub>10</sub> and PM<sub>2.5-10</sub> were highly correlated, but PM<sub>2.5-10</sub> and PM<sub>2.5</sub> were not.

There were a total of 960,041 person-years of follow-up and 36,812 incident cases of hypertension among 74,880 women eligible for analysis (incidence rate of 3,834 per 100,000 person-years). HRs and 95% CIs for each 10  $\mu$ g/m<sup>3</sup> unit change in 24-month and cumulative average predicted PM are presented in Table 3. We present linear exposure-response functions, as no statistically significant deviations from linearity were observed. In the basic models, adjusted for age, calendar year, race, and region of the country, each 10  $\mu$ g/m<sup>3</sup> increase in PM<sub>10</sub>, PM<sub>2.5</sub>, and PM<sub>2.5-10</sub> in the previous 24 months was associated with small, but statistically significant, increases in the risk of incident hypertension.. Results were similar in models using cumulative average exposures, and in multivariable models (24-month average PM<sub>10</sub> HR: 1.02, 95%CI: 1.00, 1.04; PM<sub>2.5</sub> HR: 1.04 95%CI: 1.00, 1.07; and PM<sub>2.5-10</sub> HR: 1.03, 95%CI: 1.00, 1.07). In models including both PM<sub>2.5</sub> and PM<sub>2.5-10</sub>, the results were similar to those from the single size-fraction models.

There were a total of 742,256 person-years of follow-up and 27,906 hypertension cases among the 60,416 women with information on roadway proximity. There was no evidence of elevation in risk of hypertension with living closer to a major roadway, regardless of roadway type (Table 4). No associations were observed in continuous models, or in models using alternative distance categories. There was no evidence of effect modification by moving status (data not shown).

We did not observe effect modification by diabetes, moving status, region of residence, DASH diet score, or latitude (Table 5, Supplemental Material Tables S1 and S2). However, the association of PM exposure on hypertension was modified by age and BMI. P values for interaction were statistically significant in all models with the exception of age and PM<sub>2.5-10</sub>. Higher risks were observed for younger women (<65 years old) (HR 24-month average PM<sub>10</sub>: 1.04, 95%CI: 1.01, 1.06; HR PM<sub>2.5</sub>: 1.07 95%CI: 1.02, 1.12; and HR PM<sub>2.5-10</sub>: 1.05, 95%CI: 1.01, 1.09) and for obese women (BMI ≥30) (HR 24-month average PM<sub>10</sub>: 1.07, 95%CI: 1.04, 1.12; HR PM<sub>2.5</sub>: 1.15 95%CI: 1.07, 1.23; and HR PM<sub>2.5-10</sub>: 1.13, 95%CI: 1.07, 1.19). There was a suggestion of higher risks with exposures to PM<sub>2.5</sub> before 2000.

## DISCUSSION

Long-term exposure to ambient air pollution (PM<sub>10</sub>, PM<sub>2.5</sub>, and PM<sub>2.5-10</sub>) was associated with very small, but statistically significant, increased risks of incident hypertension in this large prospective cohort study of women living throughout the contiguous United States. A 10 µg/m<sup>3</sup> increase in the 24 month moving average of all three size fractions was associated with the following multivariable adjusted HRs: (PM<sub>10</sub> HR: 1.02, 95%CI: 1.00, 1.04; PM<sub>2.5</sub> HR: 1.04

95%CI: 1.00, 1.07; and  $PM_{2.5-10}$ HR: 1.03, 95%CI: 1.00, 1.07). Similar results were observed with cumulative average exposures. In addition, associations were stronger among younger women under 65-years of age and the obese; however, there was no evidence of effect modification by diabetes, region or latitude or residence, DASH score or moving status. Roadway proximity, a proxy for overall traffic exposures, was not associated with incidence of hypertension.

Our estimated HRs for a  $10 \mu g/m^3$  increase in  $PM_{10}$ ,  $PM_{2.5}$ , and  $PM_{2.5-10}$  are lower than the associations observed in some other studies of incident hypertension. In a recent study, 35,303 non-hypertensive Canadian adults responded to population-based health surveys between 1996 and 2005 and were followed until 2010, with a total of 8,649 incident cases of hypertension (Chen et al. 2014). Each  $10 \mu g/m^3$  increase in  $PM_{2.5}$  was associated with an HR of 1.11 (95% CI, 1.03,1.20). A study of 3,236 members of the Black Women's Health Study (BWHS) living in Los Angeles who were free of hypertension at baseline, reported an incident rate ratio (IRR) for hypertension of 1.48 (95% CI, 0.95,2.31) for each  $10 \mu g/m^3$  increase in  $PM_{2.5}$ , and the association was attenuated in models that included both  $PM_{2.5}$  and  $NO_x$ , with an IRR of 1.32 (95% CI, 0.84,2.05) (Coogan et al. 2012). However, in analyses based in the full BWHS cohort (N=33,771), an interquartile range increase ( $2.9 \mu g/m^3$ ) in  $PM_{2.5}$  was associated with a multivariable adjusted HR=0.99 (95%CI: 0.93, 1.06) (Coogan et al. 2015). Individuals in the BWHS and Ontario studies tended to be younger, and a greater proportion were obese, compared to the women in our cohort. However, effect modification by age and BMI were not observed in either of the previous studies (Chen et al. 2014; Coogan et al. 2015).

A larger literature has examined the impact of a number of different air pollutants on prevalence of hypertension, and overall, most have suggested increased prevalence with increasing exposures (Babisch et al. 2014; Chen et al. 2015; Dong et al. 2013; Dong et al. 2015; Foraster et al. 2014a; Fuks et al. 2011; Johnson and Parker 2009; Sorensen et al. 2012). Increases in air pollution have also been associated with increases in the number of emergency department visits for hypertension in Edmonton, Canada (Szyszkowicz et al. 2012), and with hospital admissions for hypertension in a study from Brazil (Arbex et al. 2010).

There is a large literature concentrated on the link between air pollution and blood pressure (Auchincloss et al. 2008; Chuang et al. 2010; Chuang et al. 2011; Dai et al. 2016; Fuks et al. 2011; Giorgini et al. 2015; Hoffmann et al. 2012; Kelishadi et al. 2011; Lin and Kuo 2013; Mobasher et al. 2013; Schwartz et al. 2012; Sorensen et al. 2012; Zanobetti et al. 2004). Only a handful of these studies have focused on long-term effects (Auchincloss et al. 2008; Chan et al. 2015; Chuang et al. 2011; Foraster et al. 2014a; Foraster et al. 2014b; Fuks et al. 2011; Liu et al. 2016; Schwartz et al. 2012; Sorensen et al. 2012). Overall results have been inconsistent, although the majority of studies have observed positive associations between PM and blood pressure. These inconsistencies may be related to differences in PM composition, and the different targeted study populations (e.g. individuals with pre-hypertension (Kelishadi et al. 2011), diabetes (Hoffmann et al. 2012), or sleep-disordered breathing (Liu et al. 2016), pregnant women (Mobasher et al. 2013), or participants in cardiac rehabilitation (Zanobetti et al. 2004)).

We found no association of any of our measures of roadway proximity with incident hypertension. The evidence for roadway proximity has been mixed in the literature (Dong et al.

2013; Fuks et al. 2014; Johnson and Parker 2009; Kingsley et al. 2015; Kirwa et al. 2014; Sorensen et al. 2012). Studies assessing the association between traffic-related pollutants, such as NO<sub>2</sub>, have observed more consistently adverse effects on blood pressure and/or hypertension prevalence (Dong et al. 2013; Foraster et al. 2014a; Foraster et al. 2014b; Fuks et al. 2014; Liu et al. 2016; Schwartz et al. 2012; Sorensen et al. 2012; Zhao et al. 2013).

In stratified analyses, we observed stronger effects of air pollution among individuals under 65 years of age, in contrast to previous studies that observed no effect modification by age (Chen et al. 2014; Coogan et al. 2015). This may reflect a depletion of susceptible individuals in the older age group, or may reflect true biological differences. Literature suggests that older individuals exhibit reduced responsiveness to sympathetic and autonomic nervous system stimuli (Cohen et al. 2012; Esler et al. 1995), which could explain the differences in effect by age. It is also possible that differences in time-activity patterns between older and younger participants may explain this observation.

We observed a stronger positive association between PM and hypertension in obese participants, similar to two other studies (Dong et al. 2015; Zhao et al. 2013), which reported that obesity may amplify the association of long-term air pollution exposure with hypertension in China. The mechanism underlying the synergistic effects of PM and obesity on hypertension is not clear; one possible explanation is that obesity and exposures to PM both result in systemic inflammation (Dubowsky et al. 2006). Additionally, obese individuals have a higher inhalation rate compared to their normal weight counterparts (Brochu et al. 2014). Thus, women with a higher BMI are a potentially susceptible population, and the causal pathway warrants further exploration.

There is a large body of evidence that PM inhalation leads to elicitation of systemic inflammation, oxidative stress responses, and endothelial dysfunction, as well as imbalance of the autonomic nervous system, all of which are plausible mechanisms that may underlie associations with acute and chronic blood pressure elevations (Brook et al. 2010; Donaldson et al. 2001). If there are repeated rises in intravascular pressure, hypertrophic remodeling of the resistance vessels will cause medial thickness, which will result in a fixation of blood pressure elevations (Valavanidis et al. 2008). Components of PM, for example black carbon, have been shown to elevate blood pressure by activation of the sympathetic nervous system, direct vasoconstriction, and alterations in blood coagulability (Schwartz et al. 2012).

This study has a few key limitations. Findings may not be generalizable to the whole U.S. population, as our study participants represent a narrow range of occupation and socioeconomic status, are less obese, and are exposed to low levels of PM compared to some of the other populations studied (especially those in China). Although we used a complex spatiotemporal model to predict address-level monthly exposure estimates, we do not have information on the amount of time each participant spent at home, or the amount of ambient pollution that may have infiltrated the home, which would lead to exposure misclassification. To assess the potential impact of this error, we used measurement error correction methods (Hart et al. 2015; Liao et al. 2011) to estimate the potential impact of using ambient and not personal estimates of PM<sub>2.5</sub>. In the full cohort, using only follow-up after 2000 (a limitation of the method), the HR for a 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> was 1.07 (95%CI: 1.01, 1.14), and the measurement corrected estimate was 1.12 (95%CI: 1.00, 1.25). This suggested that we are likely underestimating the effects of

PM on hypertension. Another limitation is that since  $PM_{2.5}$  and  $PM_{2.5-10}$  were estimated from  $PM_{10}$  before 1999 (due to the sparsity of  $PM_{2.5}$  monitors) it is likely that our exposure estimates have more measurement error in the earlier portions of the study. This would limit our ability to detect associations; however, in models stratified by time period, we did not observe stronger effects for  $PM_{2.5}$  after 2000. Furthermore, roadway proximity is a weak proxy for actual traffic related exposures, such as gaseous pollutants and noise effects, likely explaining our lack of elevated findings. Additionally, limited person-time in the cohort was spent at addresses within 99 m of A1 to A3 roadways. Another limitation is that although we were able to adjust for a large number of time-varying covariates that were either known risk factors for exposure, or predictors of exposure, and overall our multivariable models were relatively insensitive to the inclusion of additional covariates. However, the large number of factors included in our multivariable models may have led to over-adjustment. In particular, the inclusion of potential mediators of the air pollution effect could be problematic. Our outcome measure also may be subject to misclassification, although our population has medical expertise, and they have been shown to provide accurate information on hypertension (Colditz et al. 1986). there may be some misclassification of outcomes. There may also be differences in diagnosis patterns that are not fully controlled for, even though our models are adjusted for region of the country and calendar year. Lastly, information on absolute levels of systolic and diastolic blood pressure are not available in the NHS cohort, therefore a weakness of our study is the reliance on the dichotomous outcome of hypertension.

This study has several strengths, including the availability of monthly estimates of three size fractions of PM at the residential addresses of all cohort members, time-varying data on potential

confounders and effect modifiers, and previously validated incidence of hypertension. Additionally, we were able to adjust for various lifestyle factors associated with hypertension, including diet, physical activity, and family history. Most importantly, with the GIS-based exposure model, we could assess exposures on a finer spatial and temporal scale than most previous studies.

## **CONCLUSION**

In conclusion, we find small, but statistically significant, associations of 24-month and cumulative average exposures to  $PM_{10}$ ,  $PM_{2.5}$ , and  $PM_{2.5-10}$  with incidence of hypertension among women in the Nurses' Health Study living throughout the United States. Associations were stronger when analyses were restricted to women under 65-years of age and the obese. There was no association between incidence of hypertension and residential roadway proximity. As hypertension is a potential risk factor for cardiovascular disease with a very high prevalence, even small changes are important at the population level.

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**Table 1. Age-standardized Characteristics of 74,880- Participants in the Nurses' Health Study throughout follow-up (1988-2008)**

Characteristic	Mean (SD) or %
Age, years <sup>a</sup>	60.39 (8.62)
24-Month Average PM <sub>10</sub> (μg/m <sup>3</sup> )	22.24 (6.64)
24-Month Average PM <sub>2.5</sub> (μg/m <sup>3</sup> )	15.61 (4.24)
24-Month Average PM <sub>2.5-10</sub> (μg/m <sup>3</sup> )	10.56 (4.80)
Body Mass Index (kg/m <sup>3</sup> )	25.27 (4.54)
Census tract median income (\$USD)	65,401 (25,730)
Census tract median home value (\$USD)	177,303 (133,832)
Race	
Caucasian	95
African-American	1
Asian	1
Other	4
Body Mass Index (kg/m <sup>3</sup> )	
<18	3
18-25	53
25-30	31
30+	13
Alcohol consumption (grams/day)	
0	31
1-4	26
5-9	9
10-14	7
15-29	5
30+	3
Missing	18
DASH diet score	
Quintile 1	17
Quintile 2	16
Quintile 3	18
Quintile 4	15
Quintile 5	16
Missing	18
Smoking Status	
Current	14
Former	41
Never	44
Physical Activity (MET-hrs/week)	
Quintile 1	15
Quintile 2	17
Quintile 3	18
Quintile 4	19

Quintile 5	19
Missing	12
Family History of Hypertension	37
Diabetes	3
Hypercholesterolemia	33
Current statin use	5
Current aspirin use (days/week)	
<1	47
1	16
2-3	7
4-5	4
6+	11
Individual level socioeconomic status	
RN degree	81
Married	72
Husband's education	
Less than high school	4
High school	28
Greater than high school	42
Mother's occupation	
Housewife	64
Outside job	36
Father's occupation	
Professional	27
Other job	73
Latitude (degrees)	
0-35	18
35-40	18
40-60	65
Region of Residence	
Northeast	52
Midwest	18
West	14
South	16

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Values are means (SD) or percentages and are standardized to the age distribution of the study population.

<sup>a</sup> Value is not age adjusted.

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**Table 2. Spearman correlations between measures of time-varying 24-month and cumulative average particulate matter exposures.**

Exposure	24-month average			Cumulative average		
	PM <sub>10</sub>	PM <sub>2.5-10</sub>	PM <sub>2.5</sub>	PM <sub>10</sub>	PM <sub>2.5-10</sub>	PM <sub>2.5</sub>
<b>24-month average</b>						
PM <sub>10</sub>	1	0.78	0.66	0.72	0.63	0.56
PM <sub>2.5-10</sub>		1	0.37	0.74	0.88	0.34
PM <sub>2.5</sub>			1	0.73	0.37	0.92
<b>Cumulative average</b>						
PM <sub>10</sub>				1	0.81	0.78
PM <sub>2.5-10</sub>					1	0.37
PM <sub>2.5</sub>						1

**Table 3. HRs (95% CIs) of the association of incident hypertension 1988-2008 with each 10  $\mu\text{g}/\text{m}^3$  increase in PM exposures among 74,880 members of the Nurses' Health Study.**

Exposure	Cases	Person-Years	Basic Model <sup>a</sup>	Multivariable Model <sup>b</sup>
Single Size Fraction Models			HR (95%CI)	HR (95%CI)
PM <sub>10</sub>				
24-Month Average	36,812	960,041	1.03 (1.01, 1.05)	1.02 (1.00, 1.04)
Cumulative Average	36,812	960,041	1.02 (1.00, 1.04)	1.02 (1.00, 1.04)
PM <sub>2.5-10</sub>				
24-Month Average	36,812	960,041	1.04 (1.01, 1.07)	1.03 (1.00, 1.07)
Cumulative Average	36,812	960,041	1.04 (1.01, 1.07)	1.03 (1.00, 1.06)
PM <sub>2.5</sub>				
24-Month Average	36,812	960,041	1.05 (1.01, 1.09)	1.04 (1.00, 1.07)
Cumulative Average	36,812	960,041	1.02 (0.99, 1.06)	1.01 (0.98, 1.05)
Two Size Fraction Models				
24-Month Average				
PM <sub>2.5-10</sub>	36,812	960,041	1.03 (0.99, 1.06)	1.02 (0.99, 1.06)
PM <sub>2.5</sub>	36,812	960,041	1.04 (1.00, 1.08)	1.03 (0.99, 1.07)
Cumulative Average				
PM <sub>2.5-10</sub>	36,812	960,041	1.03 (1.00, 1.07)	1.03 (1.00, 1.06)
PM <sub>2.5</sub>	36,812	960,041	1.01 (0.98, 1.05)	1.00 (0.97, 1.04)

<sup>a</sup> Adjusted for age, race, calendar year and region.

<sup>b</sup> Additionally adjusted for BMI, DASH diet score, alcohol consumption, smoking status, physical activity, family history of hypertension, menopausal status, non-narcotic analgesic intake, statin use, diabetes, individual level socioeconomic status (educational attainment, marital status, partner's educational attainment, and parental employment), and Census tract median income and home value.

**Table 4. HRs (95% CIs) of the association of incident hypertension 1988-2008 with roadway proximity among 60,416 members of the Nurses' Health Study.**

Exposure Category	Cases	Person-years	Basic Model <sup>a</sup> HR (95%CI)	Multivariable Model <sup>b</sup> HR (95%CI)
Distance to A1 (m)				
≥200	27,173	722,758	1.00 (Referent)	1.00 (Referent)
100-199	509	13,761	0.98 (0.90, 1.07)	0.96 (0.88, 1.05)
0-99	224	5,737	1.02 (0.89, 1.17)	1.01 (0.88, 1.15)
Continuous (per 100m)	27,906	742,256	1.00 (0.98, 1.01)	1.00 (0.98, 1.01)
Distance to A1-A2 (m)				
≥200	25,817	688,590	1.00 (Referent)	1.00 (Referent)
100-199	1,244	31,749	1.03 (0.97, 1.09)	1.03 (0.97, 1.09)
0-99	825	21,917	1.01 (0.94, 1.08)	0.97 (0.91, 1.04)
Continuous (per 100m)	27,906	742,256	0.99 (0.98, 1.00)	1.00 (0.99, 1.01)
Distance to A1-A3 (m)				
≥200	15,749	423,164	1.00 (Referent)	1.00 (Referent)
100-199	5,495	143,556	1.03 (0.97, 1.09)	1.03 (0.97, 1.09)
0-99	6,662	175,536	1.01 (0.94, 1.08)	0.97 (0.91, 1.04)
Continuous (per 100m)	27,906	742,256	0.99 (0.98, 1.00)	1.00 (0.99, 1.01)

<sup>a</sup> Adjusted for age, race, calendar year and region.

<sup>b</sup> Additionally adjusted for BMI, DASH diet score, alcohol consumption, smoking status, physical activity, family history of hypertension, menopausal status, non-narcotic analgesic intake, statin use, diabetes, individual level socioeconomic status (educational attainment, marital status, partner's educational attainment, and parental employment), and Census tract median income and home value.

**Table 5. HRs for Hypertension associated with each 10  $\mu\text{g}/\text{m}^3$  increase in  $\text{PM}_{2.5}$ , stratified by age, diabetes, obesity, region, DASH score or latitude.**

Effect Modifier	Cases	Person Years	24-Month Average HR <sup>a</sup> (95%CI)	p-value for interaction	Cumulative Average HR <sup>a</sup> (95%CI)	p-value for interaction
<b>Current Age</b>						
< 65	20,823	657,012	1.07 (1.02, 1.12)	0.02	1.05 (1.01, 1.09)	0.008
≥ 65	15,989	303,030	0.99 (0.93, 1.04)		0.96 (0.91, 1.01)	
<b>Diabetes</b>						
No	35,133	932,718	1.03 (0.99, 1.07)	0.18	1.01 (0.98, 1.04)	0.35
Yes	1,679	27,323	1.14 (0.99, 1.32)		1.08 (0.94, 1.23)	
<b>Obesity</b>						
No	28,551	822,549	1.01 (0.97, 1.05)	0.0009	1.00 (0.96, 1.03)	0.005
Yes	7,945	124,886	1.15 (1.07, 1.23)		1.10 (1.03, 1.17)	
<b>Mover</b>						
No	898,002	34,485	1.04 (1.00, 1.08)	0.59	0.90 (0.87, 0.93)	0.89
Yes	62,039	2,327	1.00 (0.88, 1.14)		0.91 (0.82, 1.01)	
<b>Time Period</b>						
1998-2000	22,094	698,971	1.05 (1.01, 1.10)	0.16	0.91 (0.88, 0.95)	0.01
2000-2008	14,718	261,071	1.00 (0.94, 1.06)		0.99 (0.94, 1.05)	
<b>Region</b>						
Northeast	19,166	503,644	1.01 (0.96, 1.07)	0.53	1.00 (0.95, 1.05)	0.74
Midwest	6,469	168,859	1.07 (0.98, 1.17)		1.06 (0.97, 1.17)	
West	4,801	130,349	1.03 (0.97, 1.09)		1.01 (0.97, 1.06)	
South	6,360	157,190	1.07 (0.98, 1.17)		1.01 (0.94, 1.09)	
<b>DASH</b>						
Q1	6,760	166,548	1.07 (0.99, 1.15)	0.57	0.92 (0.86, 0.99)	0.37
Q2	6,125	153,693	1.02 (0.94, 1.10)		0.87 (0.81, 0.94)	
Q3	6,854	173,833	1.09 (1.01, 1.18)		0.93 (0.88, 1.00)	
Q4	5,780	151,900	1.01 (0.93, 1.09)		0.87 (0.81, 0.93)	
Q5	5,819	159,579	1.05 (0.97, 1.14)		0.88 (0.83, 0.94)	
<b>Latitude</b>						
Low	6,643	169,691	1.06 (0.99, 1.13)	0.60	1.01 (0.95, 1.07)	0.99
Middle	6,525	168,986	1.03 (0.95, 1.11)		1.01 (0.95, 1.07)	
High	23,644	621,365	1.02 (0.97, 1.07)		1.01 (0.96, 1.06)	

<sup>a</sup>Adjusted for age, race, calendar year and region, BMI, DASH diet score, alcohol consumption, smoking status, physical activity, family history of hypertension, menopausal status, non-narcotic analgesic intake, statin use, diabetes, individual level socioeconomic status (educational attainment, marital status, partner's educational attainment, and parental employment), and Census tract median income and home value, as appropriate